

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
ANTHONY M. INSOGNA
JONES DAY
222 EAST 41ST STREET
NEW YORK, NY 10017

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

| | | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------|--------------------------------------------------------|
| Applicant's or agent's file reference 9516-186-228 | | Date of mailing (day/month/year) 09 AUG 2005 |
| International application No. PCT/US04/37084 | | FOR FURTHER ACTION See paragraph 2 below |
| International filing date (day/month/year) 04 November 2004 (04.11.2004) | Priority date (day/month/year) 06 November 2003 (06.11.2003) | |
| International Patent Classification (IPC) or both national classification and IPC IPC(7): A61K 31/4035, 31/52, 31/522, 38/19, 48/00 and US Cl.: 514/234.2, 263.37, 417, 251, 283, 241 | | |
| Applicant CEL GENE CORPORATION | | |

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

| | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|
| Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230 | Authorized officer Vickie Kim Telephone No. 571-272-1600 |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|

Form PCT/ISA/237 (cover sheet) (January 2004)

BEST AVAILABLE COPY

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/37084

Box No. 1 Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

BEST AVAILABLE COPY

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/37084

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|--------------------|-----|
| Novelty (N) | Claims <u>1-29</u> | YES |
| | Claims <u>NONE</u> | NO |
| Inventive step (IS) | Claims <u>NONE</u> | YES |
| | Claims <u>1-29</u> | NO |
| Industrial applicability (IA) | Claims <u>1-29</u> | YES |
| | Claims <u>NONE</u> | NO |

2. Citations and explanations:

Claims 1-29 lack an inventive step under PCT Article 33(3) as being obvious over Buschmann et al(WO99/17798) in view of Boloor et al(US2004/0242578), Muller et al(US2003/0187052), Stein et al(US2004/0067953) and Collingwood et al(US6589950).

WO'798 is related to a methods for treating mesothelioma using JNK inhibitors, see claims 14 and 21.

US'052(Muller et al) and US'950(Collingwood et al) teaches a compound having general structure encompassed by the claims 2, 5-11 wherein the patented compound is used for treating bronchogenic carcinoma and asbestosis, respectively, see US'052(paragraph 50 and figure 1 and claims) and US'950(col. column 29, compounds 141-148 and col. 13, line 54).

US '578(Boloor et al) is related to a method for treating pleural effusion using the compound having a general structure embraced by the claims 3 and 12-20, paragraphs 3 and 9-51 at pages 1-2.

US'953(Stein et al) teaches a JNK inhibitor compound having general structure embraced by the claims 4 and 21-29, and its use in the treatment of chest cancer and further teaches combination with second active agents such as IMiD or SelCid, see figures and paragraphs 1-10 and 550-553.

In light of specification(at page 1), the diseases and conditions associated with asbestos include pleural effusion, pleural thickening, asbestosis, bronchogenic carcinoma, mesothelioma. Thus, these references are taken together, the claimed invention lack inventive step and obvious over the prior art of the record.

Claims 1-29 meet the criteria set out in PCT Article 33(4), and thus the claimed invention has industrial applicability because the subject matter claimed can be made or used in industry.

BEST AVAILABLE COPY